

### **REMARKS**

Claims 27, 29-50 and 52 are pending in the present application. Claims 1-26, 28, and 51 have been canceled. Reconsideration of the application is respectfully requested in view of the following responsive remarks. For the Examiner's convenience and reference, Applicants' remarks are presented in the order in which the corresponding issues were raised in the Office Action.

In the office action of August 7, 2007, the following actions were taken:

- (1) Claim 51 was rejected under 35 U.S.C. § 101 as not being a proper process claim;
- (2) Claims 27 and 31-52 were rejected under 35 U.S.C. § 112, first paragraph, as containing matter not described in the specification;
- (3) Claim 51 was rejected under 35 U.S.C. § 112, second paragraph, as being indefinite;
- (4) Claims 27, 28, and 30 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Cserhati and Hollo, *Intl. J. Pharmaceutics* (1994) 08:69-75 (hereinafter "Cserhati") in view of Links and Lewis, *Drugs* (1999) 57(3):293-308 (hereinafter "Links") and Baumann and Preiss, *J. Chromatography* (2001) 764:173-192 (hereinafter "Baumann"); and
- (5) Claims 27-50 were rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-38 of U.S. Patent No. 7,199,111 to Daftary et al. (hereinafter "Daftary '111") in view of Links and Baumann.

It is respectfully submitted that the presently pending claims be examined and allowed. Applicants submit that each and every amendment herein, and throughout the prosecution of the present application is fully supported by the specification as originally filed, and that no new matter has been added.

#### **Claim Rejections – 35 U.S.C. § 101**

The Examiner has rejected claim 51 under 35 U.S.C. § 101 as not being a proper process claim. Specifically, the Examiner has asserted that claim 51 recites a use without setting forth any steps involved in the process. By the present amendment, claim 51 has been canceled. Applicants therefore respectfully request that this rejection be withdrawn.

### **Claim Rejections - 35 U.S.C. § 112**

Claims 27 and 31-52 stand rejected under § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner stated that the specification provides insufficient written description to support the claim.

By the present amendment, independent claim 27 includes the limitations previously recited in claim 28. These limitations parallel those previously recited in claim 2, which the Examiner has indicated are supported by the specification. Therefore, Applicants submit that independent claim 27 and all the claims dependent from it meet the written description requirements of § 112. Applicants respectfully request that the rejection of claims 27 and 31-52 be withdrawn.

Claim 51 stands rejected under § 112, 2nd paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. As discussed above, claim 51 has been canceled. Applicants therefore respectfully request that this rejection be withdrawn.

### **Claim Rejections - 35 U.S.C. § 103**

Before discussing the obviousness rejections herein, it is thought proper to briefly state what is required to sustain such a rejection. The issue under § 103 is whether the PTO has stated a case of *prima facie* obviousness. The framework for this analysis is provided in the factual inquiries set forth in *Graham v John Deere Co.*, 383 U.S. 1 (1966), which form the background for all determinations of obviousness. See also *KSR Int'l Co. v Teleflex Inc.*, 127 S. Ct. 1727 (2007).

According to the MPEP § 2142, the Examiner has the burden and must establish a case of *prima facie* obviousness by showing the prior art reference, or references combined, teach or suggest all the claim limitations in the instant application. Further, the Examiner has to establish some motivation or suggestion to combine and/or modify the references, where the motivation must arise from the references themselves, or the knowledge generally available to one of ordinary skill in the art. The Applicant respectfully asserts the Examiner has not satisfied the requirement for

establishing a case of *prima facie* obviousness in any of the rejections.

With the above background in mind, Applicants submit that the cited references do not support a *prima facie* case for obviousness.

*Cserhati in view of Links*

Claims 27-29 and 31-51 (including independent claim 27) were rejected under 35 U.S.C. § 103 as being unpatentable over Cserhati in view of Links.

The Cserhati and Links references, when combined, do not teach or suggest all of the elements of claim 27. Cserhati discusses the interactions of taxol and other anticancer drugs with hydroxypropyl- $\beta$ -cyclodextrin (HPBCD) in forming complexes. This disclosure further reports that the capacity of drugs to form inclusion complexes with HPBCD differs considerably according to chemical structure. Particularly, the intensity of interaction is reported to increase with increasing hydrophobicity of the drug. Oxazaphosphorines in accordance with the present invention are hydrophilic and even hygroscopic. For example, ifosfamide has a solubility in water of 100 mg/ml. In fact, Cserhati discusses complexation of some 23 cancer drugs with HPBCD, but does not include oxazaphosphorines. Therefore, complexing these oxazaphosphorines with HPBCD would not be obvious to one skilled in the art based on Cserhati. Furthermore, while mesna is taught in Links as a chemoprotectant, it is clear from this disclosure that mesna is administered either before or after the administration of cyclophosphamide. Pg. 305, col. 1, lines 1-5. The two drugs are stored separately and administered separately, in accordance with the current state of the art. There is no suggestion in either reference of combining mesna in a stable solution with oxazaphosphorines and HPBCD. The difficulties involved in making a ready-to-administer formulation containing cyclophosphamide or ifosfamide along with mesna are known in the art and discussed in the Applicants' specification. Given the relative doses of mesna and cyclophosphamide or ifosfamide required for efficacy, the long-felt need of such formulations are clear, particularly when continuous administration of neoplastic drug is indicated.

In view of the above, Applicants assert that the cited references do not support a *prima facie* case for obviousness of claim 27 or any of the claims depending from it.

*Cserhati in view of Links and Baumann*

Claims 27, 28, and 30 were also rejected under 35 U.S.C. § 103 as being unpatentable over Cserhati in view of Links and Baumann. Baumann is cited as teaching ifosfamide and cyclophosphamide as commonly used oxazaphosphorines in chemotherapy. However, Baumann does not remedy the deficiency of Cserhati and Links to teach or suggest a stable, parenterally administrable formulation containing both cyclophosphamide or ifosfamide and mesna. Applicants therefore assert that the cited references do not support a *prima facie* case for obviousness of pending claims 27 or 30.

The Applicant respectfully asserts the Examiner has not satisfied the requirement for establishing a case of *prima facie* obviousness in any of the above rejections. Therefore, Applicant respectfully submits that the pending claims are allowable, and urges the Examiner to withdraw the rejections.

**Double Patenting**

Claims 27-50 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of claims 1-38 of Daftary '111 in view of Links and Baumann. A terminal disclaimer is attached to overcome this rejection. The present application and the Daftary '111 patent are commonly owned.

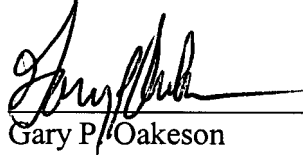
**CONCLUSION**

In light of the above, Applicant respectfully submits that pending claims 27 and 29-52 are now in condition for allowance. Therefore, Applicant requests that the rejections and objections be withdrawn, and that the claims be allowed and passed to issue. If any impediment to the allowance of these claims remains after entry of this Amendment, the Examiner is encouraged to call Gary P. Oakeson at (801) 566-6633 so that such matters may be resolved as expeditiously as possible.

The Commissioner is hereby authorized to charge any additional fee or to credit any overpayment in connection with this Amendment to Deposit Account No. 20-0100.

DATED this 6<sup>th</sup> day of November, 2007.

Respectfully submitted,



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